# EVALUATION OF EFFECT OF IMMEDIATE POSTPARTUM CURETTAGE ON RECOVERY OF ECLAMPSIA

**DISSERTATION SUBMITTED FOR THE DEGREE OF**

## *M.D. BRANCH – II*

## *OBSTETRICS AND GYNAECOLOGY*

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**CHENNAI, TAMILNADU**

## BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"EVALUATION OF EFFECT OF IMMEDIATE POSTPARTUM CURETTAGE ON RECOVERY OF ECLAMPSIA"** is bonafide record work done by **Dr. T. KAVITHA** under my direct supervision and guidance, submitted to the Tamil Nadu Dr. M.G.R. Medical University in partial fulfillment of University regulation for MD, Branch II –Obstetrics & Gynaecology.

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## DECLARATION

I **Dr. T. KAVITHA** solemnly declare that the dissertation titled **"EVALUATION OF EFFECT OF IMMEDIATE POSTPARTUM CURETTAGE ON RECOVERY OF ECLAMPSIA"** has been prepared by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any other University board either in India or abroad.

This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of MD. degree Branch – II (Obstetrics & Gynaecology) to be held in March 2008.

**Place :** Madurai **Dr. T. KAVITHA**

**Date :**

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# CONTENTS

# INTRODUCTION

Eclampsia is a form of Hypertensive encephalopathy with generalised convulsions associated with signs of preeclampsia during pregnancy, labour (or) within 7 days of delivery and not caused by epilepsy (or) other convulsive disorders. It is one of the important causes of mortality and morbidity during pregnancy, child birth& puerperium.

Of the estimated 7,00,000 maternal deaths every year world wide 10% to 15% are associated with Hypertensive disorders of pregnancy.

The incidence of eclampsia in developing countries is 0.5-2% but 4.9% per 10,000 in United Kingdom and 1 in 2000 in Europe and developed countries.

Eclampsia accounts for 50,000 maternal deaths a year world wide.

The maternal case fatality rate is 1.8% and 35% of eclamptics will have one major complication.

Perinatal mortality rate in developed countries is less than 10/1000 births to as high as 80 (or) more/1000 births in developing countries.

The Collaborative Eclampsia Trial group found that the incidence of

perinatal mortality in eclampsia ranges from 224 to 307/1000 cases of Eclampsia. According to Mudhaliar, perinatal mortality in Eclampsia is 300-600/1000 cases of Eclampsia. The overall PNMR-Eclampsia is 363/1000 cases of Eclampsia.

The presence of a toxin, that acts as a pressor substance (hysterotonin) in the deciduas and amniotic fluid of women has been suggested to be responsible for the multiplicity of clinical expression. To effect a cure, the chorionic villi must be expelled or surgically removed. Resolution of eclampsia occurs only with delivery and subsequent removal of functioning trophoblastic tissue. Accelerated recovery from the disease process following delivery could avert associated serious and life threatening maternal complications and shorten the time required for intensive care and hospitalization. The present study evaluates the effect of immediate post partum curettage on the resolution of clinical and laboratory indices associated with eclampsia.

## AIM OF THE STUDY

- To evaluate the effect of immediate postpartum curettage upon maternal recovery from eclampsia.

# REVIEW OF LITERATURE

**Definition:-**

Preeclampsia complicated by generalized tonic-clonic convulsions is termed eclampsia. Fatal coma without convulsions also called as eclampsia, however it is better to limit the diagnosis to woman with convulsions and to regard deaths in non convulsive cases as due to severe preeclampsia.

Depending on whether convulsions appear before, during (or) after labour, eclampsia is designated as Antepartum, Intrapartum (or) Post partum.

**Etiology:**

Etiology of Pregnancy induced Hypertension.

**1)Abnormal trophoblastic Invasion:**

In pre eclampsia, there is incomplete trophoblastic invasion of uterine spiral arteries. Endothelial damage, insudation of plasma constituents into vessel wall, proliferation of myointimal cells &medial necrosis are observed.

Lipid laden myointimal cells and macrophages – atherosis causes obstruction of spiral arterioles.

**2) Immunological Factors:-**

The risk of preeclampsia is enhanced where formation of Blocking

Antibodies to placental antigenic sites might be impaired. They arise where effective immunization by previous pregnancy is lacking as in first pregnancy (or) in multiple pregnancy where number of Antigenic sites provided by the placenta is great compared to the amount of antibody—Beer(1978)

Bardeguez and associates (1991) –woman who develop preeclampsia have lower proportion of helper T cells ($Th_1$) than normotensive woman. Th1/Th2 imbalance with Th2 dominance may be mediated by adenosine, which is higher in serum of preeclampsia woman than normotensives.

Preeclampsia common in woman with anticardiolipin antibodies, Antibodies associated with b2 glycoprotein 1 appear more relevant. Immune complexes and anti endothelial cell antibodies may also be involved. (Taylor and Roberts,1999)

**3)Genetic Factors:-**

Ness (2003) suggested that the tendency for preeclampsia is inherited. Cooper and Liston (1979) suggested that susceptibility to pregnancy induced Hypertension is due to single recessive gene Chesley and Cooper (1986) suggested single gene model. Trogstad and coworkders (2004) suggested polygenic inheritance. Kilpatrick and associates (1989) showed association

between HLA-DR4 and proteinuric Hypertension.

Ward and Zhang (2003) reported that woman heterozygous for angiotensinogen gene variant T235 had a higher incidence of preeclampsia of fetal growth restriction. Morgan and colleagues (1995,1999) did not confirm this, but they found that woman homozygous for the mutation had abnormal trophoblastic invasion.

Polymorphisms of genes for TNF, Lymphotoxin-a and inteleukin –1b have been studied with varying results (Helfer; Kacgneuher; Livingstor 2001). Dizon Townsend and colleagues (1996) found higher incidence of factorV leiden mutations in pregnancy induced hypertensive woman.

**4) Nutritional factors:-**

A number of dietary deficiencies (or) excess have been blamed as a cause of eclampsia. Dietary taboos included are meat, protein, purines, fat, dairy products, salt and others.

John and coworkers (2002) showed that a diet rich in fruits and vegetables have antioxidant activity with decreased blood pressure.

Zhang and associates showed that the incidence of preeclampsia was doubled in Woman whose daily intake of ascorbic acid was less than 85mg.

Carroli and colleagues (1994) implicated that calcium supplementation reduces the risk of preeclampsia.

Belizan91991),Lopez-Jeramillo (1989), Sanchez-Ramos(1194) and their associates reported that mid pregnancy daily dietary supplementation of 2gm calcium significantly reduced the incidence of Hypertension.

**5)Vasculopathy and the inflammatory Changes:-**

In response to placental factors released by ischemic changes, (or) any other inciting cause, a cascade of events is set in motion (Redman and Sargent 2003)

Staff and colleagues 1999 - suggested that the decidua also contains an abundance of cells when activated, can release noxious agents. They serve as mediators to provoke endothelial cell injury.

Fass and colleagues 2000 and Gervasi 2001, showed that preeclampsia is due to an extreme state of activated leucocytes in maternal circulation.

TNF- α and their interleukins may contribute to the Oxidative stress associated with preeclampsia.

Oxidative stress produce highly toxic radicals and injure endothelial cells(Manten and associates 2005) modify their nitric oxide production and

interfere with prostaglandin balance.

## PATHOGENESIS

### 1) Vasopasm:

The concept of vasopasm was advanced by volhard (1918) based on direct observation of small vessels in nail beds, ocular fundi and bulbar conjunctiva. Wang and colleagues (2002) demonstrated disruption of endothelial junctional proteins. Suzuki and co workers (2003) demonstrated ultra structural changes in sub endothelial region of resistance arteries in preeclamptic woman. Vasospasm may be worse in HELLP syndrome-Fischer and colleagues, 2000.

### 2) Endothelial cell activation:-

Hayman, Roberts, Walker 2000 showed that clinical syndrome of preeclampsia result from widespread endothelial cell changes.

### (i) Increased Pressor responses:-

Abdul—Karim and Assali 1966 showed that normal pregnant woman develop refractoriness to infused Vasopressors.

Woman with early preeclampsia, have increased vascular reactivity to infused nor epinephrine and angiotensin II. (Raab and co workers 1956. Talledo and associates, 1968)

**ii) Prostaglandins:-**

Taylor and Roberts (1999) showed that endothelial prostacyclin production is decreased in preeclampsia that is mediated by phospholipase A2.

Platelet thromboxane A2 increases and the prostacyclin: thromboxane A2 ratio decreases. That favours increased sensitivity to angiotensin II that ends in Vaso constriction.

Chavarria (2003) given the evidence that these changes are apparent as early as 22 weeks in woman who later develop preeclampsia.

**iii) Nitric Oxide:**

A potent vasodilator synthesized from L-arginine by endothelial cells. It is the compound that maintains normal low pressure vasodilator state characteristic of Feto placental perfusion-Myatt and co workers 1992.

Wang and colleagues showed that preeclampsia is associated with decreased endothelial nitric oxide synthase expression, which increases cell

permeability. It's production increased as compensatory mechanism in severe preeclampsia. So increased serum concentration of nitric oxide is likely the result of hypertension, not the cause – Morris and colleagues 1996.

**iv) Endothelins:**

Mastrogiannis and coworkers showed that these 21 amino acid peptides are potent vaso constrictors, and endothelin -1 (ET-I) is primary isoform produced by human endothelium.

Taylor and Roberts (1999) showed that the placenta is not the source of increased ET-I.

Sagsoz and Kucukozkan 2003 observed that treatment of preeclamptic woman with magnesium sulphate lowers ET-I concentrations.

**v) Angiogenic Factors:**

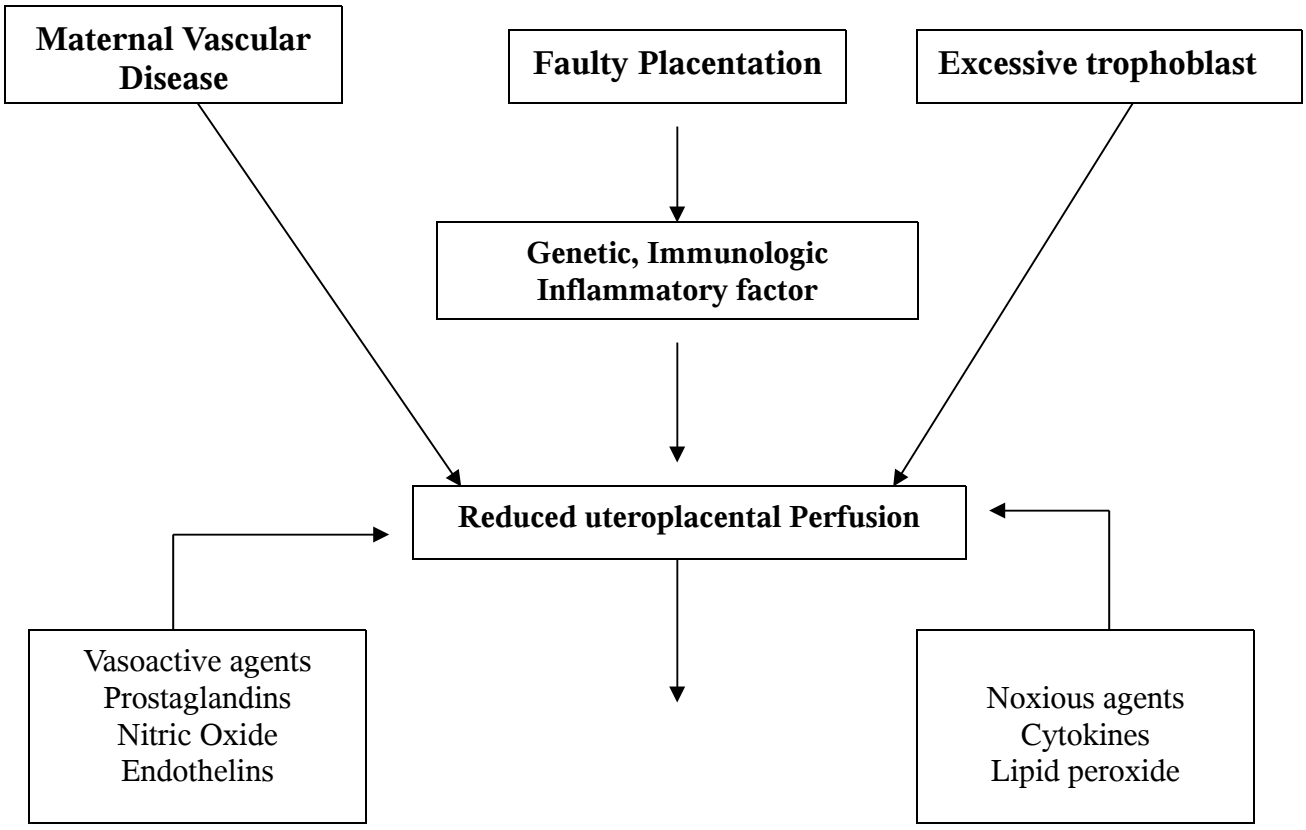
Vascular endothelial growth factor (VEGF) and placental growth factor (PIGF), the glycosylated Glycoproteins are selectively mitogenic to endothelial cells.

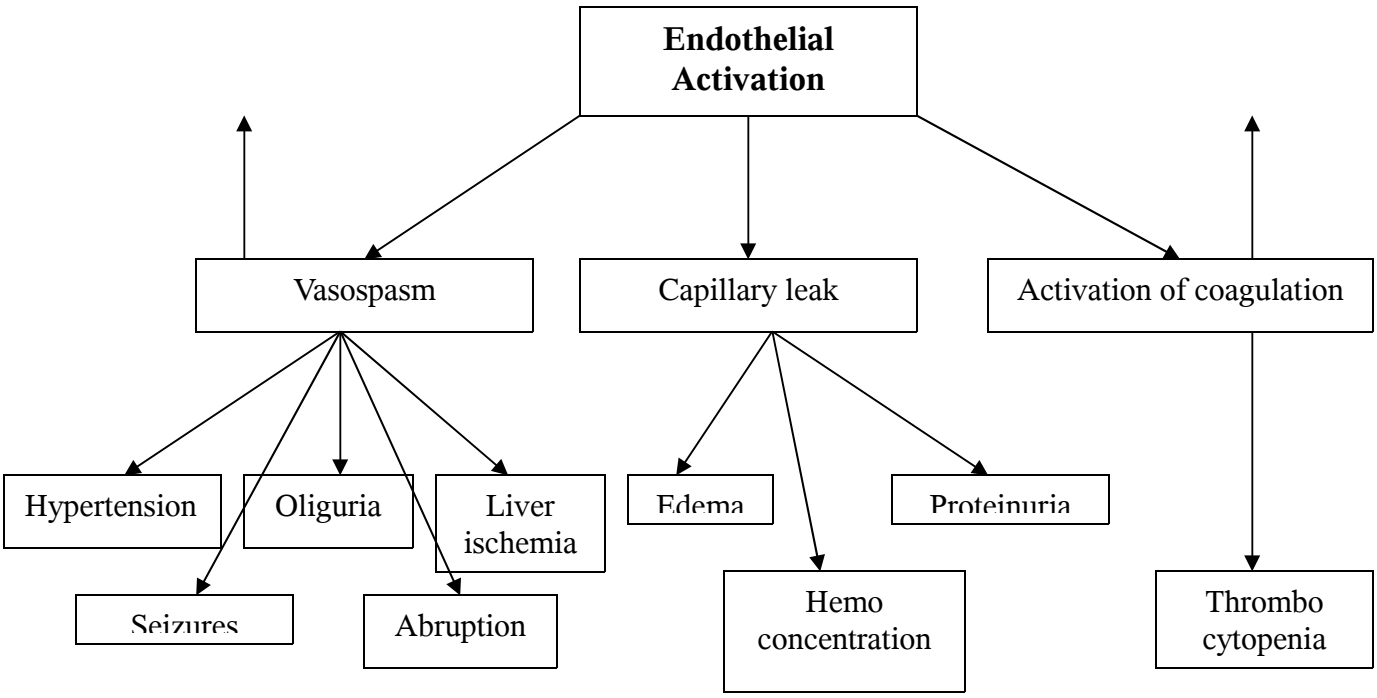
Simmons and co workers 2000 showed the VEGF is increased in serum

from woman with preeclampsia but the bioavailability is decreased.

In Preeclampsia, the gene for Soluable Fms-Like tynosine kinase 1 (SFLt) is upregulated –Maynard &associates.

## PATHOPHYSIOLOGY






**Clinical Course of eclampsia**

Eclampsia is most common in last trimester and becomes more frequent as term approaches.

Maternal hypoxia and lactic acidosis caused by convulsions, the fetus develops bradycardia, pulmonary edema may occur. Sudden death due to massive cerebral hemorrhage can occur. 10% of cases had blindness due to retinal detachment (or) occipital lobe ischemia and edema. Rarely eclampsia is followed by psychosis.

**Differential diagnosis:-**

Epilepsy, encephalitis, meningitis, cerebral tumor, cysticercosis and ruptured cerebral aneurysm.

**Complications of Eclampsia:**

Placental abruptions (10%), Neurological deficits (7%) Aspiration pneumonia (7%) pulmonary edema (5%) cardiopulmonary arrest (4%) Acute renal failure (4%) maternal death (1%).

## MANAGEMENT

### 1.General management

It plays an important role in the management of eclampsia. The patient is nursed in a quiet room with a medical or nursing attendant always present. Pulse rate, respiration, blood pressure, colour, restlessness, urine output must be constantly observed. A mouth gag, airway and $O_2$ must be available. Patient is put in left lateral position in a railed cot. Throat is cleared of secretions and vomitus by intermittent suction. A soft firm mouth gag introduced in time will save injury to the tongue. An indwelling catheter in the bladder will give an accurate assessment of the urine output and will also prevent restlessness due to a full bladder (Dewhurst 1984.) Blood pressure is measured half hourly till it is controlled and then second hourly. A record of grade of consciousness is maintained. Nutrition and hydration are maintained parenterally.

### II. Anticonvulsant line of Management

### History

In the early years of the $20^{th}$ century early intervention to achieve

delivery was widely practiced. The mortality was very high. Later in 1930, Strongonoff introduced his conservative regimen of heavy sedation with morphia by injection, and chloral or bromide per rectum gave better results. Once the convulsions were fully controlled the membrane were ruptured.

In 1920-30 stomach and colonic lavage with magnesium sulphate was used to clear the patient of toxins and sedation with chloroform.

In 1951-1960 barbiturates were used. 'O' Donnel Browned used continuous thiopentone in 20% dextrose, but causes marked cerebral depression.

In 1961, lytic cocktail regimen using pethidine, chlorpromazine and promathazine was introduced by Dr. M.K.K.Menon. He treated 1448 cases. Recurrence of fits was 15%. Maternal mortality was 2.4%.

Nager et al (1988) treated 98 cases with lytic cocktail (LC) with maternal mortality rate of 8.2%.

Llewellyn Jones (1961) conducted a study on 150 cases of eclampsia with lytilcocktail and the maternal mortality was 6.6%.

Lopez Liera used lyticocktail on 120 eclmaptic women and the maternal mortality was 11.7%.

Lean et al (1968) have reported excellent results with large doses of chlordiazepoxide or diazepam.

Magnesium sulphate was first used by Horn in Germany in 1906 intrathecally. In 1926 intravenous regimen of magnesium sulphate was reported by Lazard in Los Angeles and intramuscular regimen by Dorsett in St. Louis. However the popular intra muscular regimen of Pritchard was introduced in 1955 and intravenous regimen by Zuspan in 1964.

Phenytoin Sodium was introduced in management of eclampsia in 1987.

## DOSAGE SCHEDULE OF VARIOUS REGIMENS

1. **Menon's Regimen (1961)**

**0 Hours**

25 mg chlorpromazine and 100 mg pethidine in 20 ml of 5% glucose given intravenously. 50 mg chlorpromazine and 25 mg promethazine given intramuscularly.

A drip of 20% dextrose containing 200 mg pethidine is set up and run slowly at a rate of 20-30 drops/minute.

| | | |
|---|---|---|
| 0-4 hrs | Promethazine | 25 mg Im |
| 0-8 hrs | Chlorpromazine | 50 mg Im |
| 0-12 hrs | Promethazine | 25 mgIm |
| 0-16 hrs | Chlorpromazine | 50 mg Im |
| 0-20 hrs | Promethazine | 25 mg Im |
| 0-24 hrs | Chlorpromazine | 50 mg Im |
| 0-28 hrs | Promethazine | 25 mg Im |
| 0-32 hrs | Chlorpromazine | 50 mg Im |
| 0-36 hrs | Promethazine | 25 mg Im |
| 0-40 hrs | Chlorpromazine | 50 mg Im |
| 0-44 hrs | Promethazine | 25 mg Im |
| 0-48 hrs | Chlorpromazine | 50 mg Im |

Menon (1961) used lyticocktail in 1448 eclamptic women and maternal mortality was 2.2%.

Llewllyn Jones (1961) in his study using lyticcocktail had a maternal mortality of 6.6%. Lopez Liera (1982) in his study had a maternal mortality of 11.7%. Bhalla et al (1994) in his study using lyticcocktail had a maternal mortality of 4.4%.

**2. Diazepam(1968)**

A loading dose of 10 mg diazepam intravenously over 2 minutes followed by an intravenous infusion of 40 mg in 500 ml normal saline for 24 hours. Rate of infusion titrated against level of consciousness with the aim of

keeping the woman sedated but arousable. Diazepam can cause respiratory depression. It is poorly excreted by the neonate which tends to be sedated, hypothermic and unable to breast feed for several days.

3. **Chlordiazepoxide (1968)**

An initial intravenous injection of 10 mg followed by a continous injection of 100 mg in 500 ml of 5% dextrose at a rate of 30 drops/ minute or titrated according to the sedation needed.

4. **Clonazepam (1977)**

1 mg intra venous bolus followed by an intravenous infusion of 2.5mg in 500 ml of 5% dextrose.

5. **Chlormethiazole (Duffs et al 1968)**

It is an effective anticonvulsant. Intra venous infusion of 0.8% chlormethiazone in 500 ml of 5% dextrose at a rate of 2-4 gm/hours for first 5-10 minutes and 0.5-1 gm/hour thereafter to produce easily arousable sleep. It has a short half life of 45 minutes, so does not produce prolonged sedation in the mother or neonate.

6. **Magnesium Sulphate ($MgSo_4$)**

In 1955 Prichard initiated a standardized treatment regimen at Parkland

Hospital.

In 1964 Zuspan initiated the intravenous magnesium sulphate regimen.

**a) Pritchard Regimen**

| **Loading Dose** | **Maintenance Dose** |
|---|---|
| 4 g of 20% $MgSo_4$ IV at a rate of exceeding 1 g/ min | Every 4 hrs 5 gm of 50% $MgSo_4$ as IM on alternate buttocks after assuring |
| 10 g of 50% $MgSo_4$ deep IM in buttocks | a) Patellar reflex is present<br>b) Respiration are not depressed >16/ minute<br>c) Urine output > 100 ml in preceding 4 hours |
| If convulsions persists after 15 minutes, give 2 g of 20% $MgSo_4$ at a rate not exceeding 1 gm/ minute | $MgSo_4$ discontinued 24 hours after delivery |
| **b) Zuspan's Regimen (1964)** | |
| **Loading Due** | **Maintenance Dose** |
| 4 g of 20% $MgSo_4$ IV at a rate not exceeding 1g /min | 1-2 g /hour by controlled infusion pump for 24 hours after delivery (concentration not to exceed 20%) |

**c) University of Tennessee guidelines for intravenous $mgso_4$**

**Loading Dose**

Give 30ml of 20% $mgso_4$ solution (6g) in 100ml of 5% dextrose over

10 to 15 minutes.

**Maintenance Dose:**

Add 20g of $mgso_4$ (Four 10 ml ampoules of 50% solution to 1000ml of 5% Dextrose and give intravenously at a rate of 100ml/hour (2g/hour0. Adjust the rate of infusion to keep serum magnesium levels between 4.8 & 9.6 mg/dl.

If serum magnesium levels are available the dose is adjusted according to the patellar reflex and urine output in previous 4 hour period.

**Monitoring of Magnesium Toxicity:**

- Urine output atleast 30ml/hour
- Deep tendon reflexes should be present.
- Respiratory rate should exceed 14/min.

## PHARMACOKINETICS

### Magnesium Sulphate

It has a molecular weight of 246. 1 gm of magnesium sulphate has 98mg of elemental magnesium.

### Distribution and Plasma levels

Infused magnesium sulphate is distributed rapidly throughout the entire

extra cellular fluid space and some is taken up by bone but none by red blood cells. Intravenous loading due of 4-6 gm results in immediate plasma concentration of 5-9mg/dl and it falls to 3-4mg/dl in 60 minutes. Within 90 minutes 50% of infused magnesium moves into bones and other cells. By 4hours 50% of infused Magnesium is excreted in the urine.

**Excretion**

Magnesium is excreted almost solely by the Kidneys. 50% of the infused dose is excreted after 4 hours in urine. 99% of the bolus intravenous dose is excreted within 24hours.

**Mechanism of action**

Some believe its action to be mainly peripheral at the neuro muscular junction with minimal central effects. While some believe that the main action is central. Calcium entry into neurons is regulated by specific excitatory amino acid linked channels. Excitatory amino acids such as L-glutamate and L-aspartate are the major neuro transmitters in mammalian central nervous system. These neurotransmitters produce their effects by interacting with certain receptors on the cell surface, the excitatory amino acid receptors, N-methyl D-aspartate (NMDA) is the best characterized

excitatory amino acid receptor sub type. NMDA receptor has its channel blocked by magnesium ion and thus blocking neuronal calcium influx. Thus magnesium has a central nervous system effect in blocking the seizure. Cotton and associates (1992)9 have shown that hippocampal seizures could be blocked by magnesium

Magnesium sulphate is a potent vasodilator especially in cerebral vasculature thus relieving cerebral vasospasm which is thought to be a cause for eclampsia.

**Other Actions**

- Vaso dilatation in Vascular beds
- Increased uterine blood flow (Harbert&collegues)
- Increased renal blood flow
- Increased prostocyclin release by endothelial cells (Watson and Colleagues)
- Decreased plasma rennin activity
- Decreased angiotensin converting enzyme levels
- Attentuation of vascular response to pressor substances
- Bronchodilatation

- Reduced platelet aggregation

**Pharmacological effects**

- Anti convulsant action
- Transient hypotensive effect
- Transient but mild decrease in frequency of uterine contractions but no change in the intensity of contractions.
- Clinically insignificant decrease in short term variability of fetal heart rate
- No change in long term variability of fetal heart rate or fetal heart rate accelerations

**Side Effects**

First sign of magnesium toxicity is usually the loss of patellar reflexes that occurs usually at about 9-12mg/dl because of curariform action. So maintenance dose of $MgSO_4$ is not to be given in the absence of patellar reflexes.

Early signs and symptoms of magnesium toxicity include nausea, feeling of warmth, flushing, somnolence, double vision, slurred speech and

weakness. These symptoms usually develop at plasma levels of 9 to 12mg/dl.

Muscle paralysis and respiratory arrest develop at plasma level of 15-17mg/dl. Hence respiratory rate is monitored closely.

Cardiac arrest develops at level of 30-35mg/dl. Thus it is important to keep an ampoule containing 1 gram of calcium gluconate at the bedside for intravenous administration as an antidote in case of magnesium toxicity.

Tracheal intubation and mechanical ventilation for severe respiratory depression (or) arrest. There is a transient decrease in uterine activity during intravenous injection alone. It can cause a transient decrease in fetal heart rate variability, neonatal neuro muscular and respiratory depression hyporeflexia and low apgar scores. These effects were reported in preterm infants in association with fetal growth retardation. In addition several recent studies reported no ill effects in term infants. It can cause excessive blood loss after delivery.

**Efficacy and Safety**

Rapidly effective, reliable & predictable duration of action, wide safety margin, non depressive and non toxic to the mother and baby, simple to administer and monitor in the clinical setting and readily available antidote.

Serum magnesium can be measured to ensure therapeutic concentration but many practitioners are happy to omit biochemical monitoring because of its wide margin of safety.

Duley et al (1995) in his study used clinical evaluation alone and showed that the there is no need to check serum magnesium levels. Estimation of magnesium levels are useful in the management of treatment failures.

Drug interactions with Magnesium Sulphate

| Agent | Effect | Recommendation |
|---|---|---|
| Depolarising / non Depolarizing neuro Muscular blockers | Increased activity of These agents | May need dosage reduction of neuro muscular blocking agents |
| CNS depressants eg opioids, barbiturates, general anaesthetics | Additive CNS Depression | May require dose reduction of CNS depressants |
| Nifedipine | Hypotension | Administer with caution and adjust nifedipine dosage if necessary |

At the neuromuscular junction magnesium decreases the presynaptic release of acetylcholine and reduces the sensitivity of the post junctional membrane(motor end plate). Ghoneim and long reported that the action of

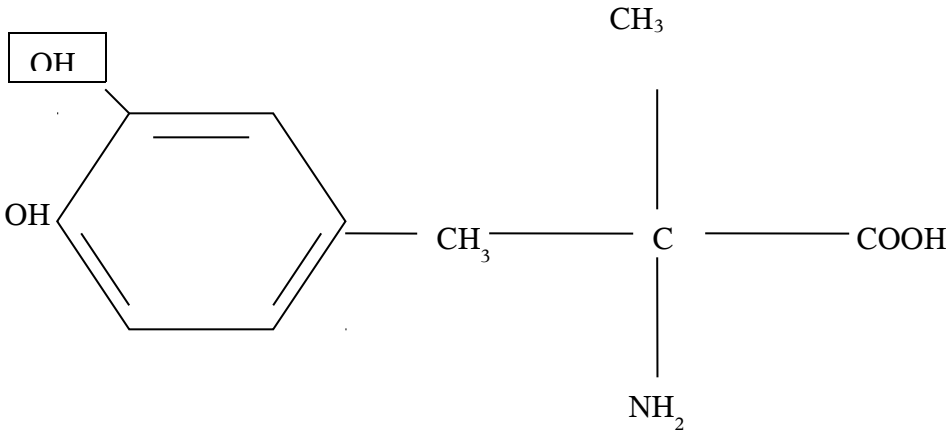
succinylcholine (non depolarizing agent)are potentiated by magnesium sulphate. A single dose of succinycholine can be safely used to facilitate tracheal intubation but may not apply when repeated dose of succinyl choline are used.

When a patient is simulataneously exposed to magnesium sulphate and nifedipine some interaction might be expected as both are calcium channel blockers. Fenakel et al (1998) studied nifedipine in women who are receiving magnesium sulphate and found effective blood pressure control in 96% women without hypertension. It would appear that while a theoretical risk of interaction could exist in practice this is relatively uncommon.

## III – Antihypertensives

### Alpha Methyl dopa

This was introduced to treat hypertension in 1960 by sjoderdesma



**Pharmacological action**

After oral (or) intravenous administration the hypotensive effect appears after 3 to 6 hours and 1-2 hours respectively. Hypotensive effect is associated with reduced cardiac output and total peripheral resistance. It does not reduce renal blood flow.

**Mechanism of action**

1. Inhibits adrenergic receptors in the vasomotor center
2. Inhibits rennin release by the kidneys

**Absorption and Excretion**

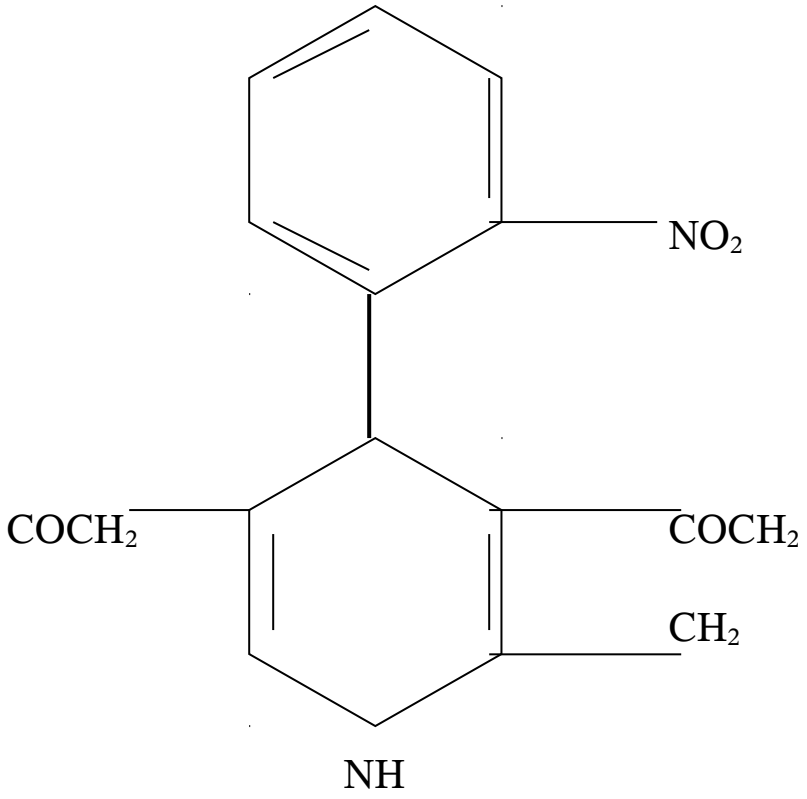
It is well absorbed orally and completely excreted in urine in 12 hours.

**Adverse Effects**

It commonly produces sedation, headache and fatigue. Other side effects are diminished Intellectual drive, drowsiness, forgetfulness, nightmares, parkinsonism, lactation and depression. Tolerance to antihypertensive effect is common. It can cause drug fever, altered liver function test (or) cholestatic jaundice. Rarely agranulocytosis, thrombocytopenia, gastrointestinal tract upset, constipation and skin rashes.

**Nifedipine**

It a calcium blocker, introduced in clinical practice in 1970 by Flerk, and Entus in 1971.




PHARMACOLOGICAL ACTIONS

It blocks the calcium transport through voltage dependent channel and thus inhibits the entry of extra cellular calcium ion necessary for the excitation contraction coupling in both the skeletal muscle and smooth muscle. It has a negative inotropic action on heart, relaxes the vascular smooth muscle in systemic as well as pulmonary circulation. Thus decreases the vascular resistance and the blood pressure. If causes a reflex tachycardia. It can be used orally or sublingually.

**Side effects**

It produces headache, tachycardia, dizziness, fatigue, orthostatic hypotension, leg cramps and skin rashes.

**Interactions**

Some have advised caution while using nifedipine with magnesium sulphate as both are calcium channel blockers, which may have a depressive effect on blood pressure.

Fenakel et al(1998) studied nifedipine in women who were receiving magnesium sulphate and found effective blood pressure control in 96% women without undesirable side effects and no cases of hypotension. It would therefore appear that while a theoretical risk of interaction does exist. In practice this is uncommon.

Bhalla et al (1994) in his study used nifedipine and magnesium sulphate and had a good control of blood pressure.

**Other Antihypertensives**

Intravenous hydrallizine (or) intravenous labetalol produces remarkably effective control of the high blood pressure.

**OBSTETRIC MANAGEMENT**

After stabilizing the patient a detailed obstetric examination made. If she is in labour, amniotomy done and oxytocin infusion started. If she is not in labour, induction with prostaglandin $E_2$ gel done for a favourable cervical score. Cesarean section done for obstetric indication or for failure of medical treatment.

**I stage :**

During labour fetal heart rate ausculated every fifteen minutes, blood pressure recorded every 2nd hourly. Intake, output maintained strictly. Maternal pulse recorded hourly. Cardiovascular system and respiratory system ausculated every 2nd hourly. Intravenous fluids preferably Ringer lactate infused at a rate of 1 ml/kg/hour.

**II stage :** Cut short by forceps, if indicated

**III stage :**

Prophylactic methyl ergometrine usually avoided to prevent the rise in blood pressure.

Blood pressure recorded every 2nd hourly until controlled and then every 4th hourly for 48hours. All other vital signs and urine output recorded every second hourly for 48 hours after delivery.

## LABORATORY FINDINGS IN PRE ECLAMPSIA :

The laboratory changes reflect the effects of the pre eclampsia on the kidney, liver foetoplacental units and in some cases, the haematological elements.

### 1. Altered Renal function :

In severe pre eclampsia, there are elevation in Serum creatinine, Blood urea nitrogen and Uric acid levels as well as decrease in creatinine clearance, proteinuria and changes in the urinary sediment.

| S.No. | | Normal Pregnancies | Pre eclampsia |
|---|---|---|---|
| 1. | Sr. Creatinine | 0.8 mg/dl or less | 1.3 to 1.4 mg/dl |
| 2. | Urea | 15 mg % | 20-25 mg% |
| 3. | Creatinine clearance | 130 ml / min or more | 100 ml / min or less |

There are many postulations that state uric acid elevation is a specific laboratory finding in pre eclampsia and uric acid levels normally decreases at the beginning of pregnancies, remain low during the second trimester, nearly reaching non-pregnant levels at term. Marked elevation of uric acid, urea and creatinine occur only with severe pre eclampsia.

**Changes in liver function tests :**

Patients with severe pre eclampsia show marked increase in SGPT, SGOT and LDH. The raised total LDH is usually reflected in the elevations of isoenzyme 5 (LDH liver). If haemolytic anaemia is also present, the electrophoretic pattern will show elevation of isoenzymes, 1,2 and 5. After delivery, SGPT and SGOT levels rapidly decrease and in most cases reach normal levels by the fifth post partum day. LDH fall more slowly and normal values are reached by post partum day eight to ten.

**Haematologic Abnormalities :**

1. Elevation of haemoglobin and haematocrit caused by characteristic decrease in plasma volume.
2. Thrombocytopenia : Pritchard et al found 26% of 91 eclamptic patients found to have platelet counts below 1,50,000. 17% had platelet count below 1,00,000 and 3% had platelet count below 50,000.
3. The plasma fibrinogen concentration is usually normal or slightly increased and it is unusual to find a fibrinogen level below 200 mg% unless the clinical course is complicated by abruption placenta.

4. The thrombin time may also be altered in eclampsia patients and it is likely to be prolonged in about 50% of these patients with severe forms of preeclampsia. This change is peculiar because it may occur in patients with normal fibrinogen concentration and normal level of fibrinogen split products.

5. Pre eclamptic patients with positive D. dimer (>0.5mg%) have a more severe form of the disease than those with a negative test.

HELLP SYNDROME :

It is an acronym proposed by Weinst to describe the clinical condition characterized by Hemolytic anaemia, elevated liver enzymes and low platelet count. The criteria for the diagnosis as defined by sibai are :

**Haemolysis :**

Schistiocytes in the blood smears

Bilirubin > 1.2 ml/dl

Absent plasma haptoglobulin

**Elevated liver enzymes :**

SGOT > 72 IU / L

SGPT > 600 IU/L

**Low platelet count**

Platelet $< 100 \times 10^3 / mm^3$

This condition has to be differentiated from thrombotic thrombocytic purpura (TTP) because their clinical, laboratory and histological characteristics are similar. Every hypertensive pregnant patient with haematological complications must be managed as if the process were included by pregnancy. This implies delivery and most cases the patient will improve rapidly post partum.

## SUBJECTS AND METHODS

The subjects of this study were 50 pregnant women who presented to labour and delivery department, Government Rajaji Hospital in the time period between January 2007 to September 2007 with physical findings of eclampsia.

At admission, evaluation included mean arterial pressure (MAP), haemoglobin, Urine – albumin, Uric acid, quantitative platelet count, Sr. creatinine, Liver function tests and examination of the fundus. As a routine location of placenta was recorded at antepartum sonography.

25 patients underwent uterine curettage after vaginal or caesarean delivery immediately after delivery of placenta under sedation with promethazine hydrochloride. At caesarean, the presumed area of the decidua basalis were curetted with large placenta curette. Patients who delivered vaginally were curetted under i.v. sedation using a placenta curette.

All curettage specimens were sent for pathological examination.

During the immediate puerperium, all subjects were observed in the obstetric intensive care unit until disease remission was apparent. Intensive postpartum surveillance maintained for 24 hours and included hourly

measurement of MAP, hourly urine output, hemoglobin with platelet count, uric acid and creatinine assessment at 24 hours. Recurrence of convulsions or other complications was noted and duration of stay in the ICU recorded.

All medications given in the obstetric room were recorded. All women with eclampsia and imminent eclampsia received Magnesium sulphate. None of the patients received fluid challenge in the recovery room. Discharge criteria from the area included.

1. Adequate diuresis (output > 100 ml / hour sustained for atleast 2 consecutive hours)
2. Blood pressure control with diastolic values below 100 ml Hg and systolic below 160 mm hg.

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2002).

Using this software, frequencies, percentage, range, mean, standard deviation $x^2$ and 'p' values were calculated. A 'p' value less than 0.05 is taken to denote significant relationship.

## RESULTS

### A. Profile of cases studied

**Table 1 : Age Distribution**

| Age in Years | No of cases in | | | |
|---|---|---|---|---|
| | Group A | | Group B | |
| | No | % | No | % |
| Less than 20 | 3 | 12 | 2 | 8 |
| 20 – 24 | 18 | 72 | 17 | 68 |
| 25 – 29 | 1 | 4 | 3 | 12 |
| 30 & above | 3 | 12 | 3 | 13 |
| Total | 25 | 100 | 25 | 100 |
| Mean | 22.64 | | 22.96 | |
| S.D | 4.64 | | 3.96 | |
| P | 0.3314 (Not Significant) | | | |

The mean age of the cases in both the groups does not differ significantly.

70% of the patients belong to age group of 20-24 years

**Table : 2 Parity**

| Parity | No of cases in |
|---|---|

| | Group A | | Group B | |
|---|---|---|---|---|
| | **No** | **%** | **No** | **%** |
| Primi | 18 | 72 | 15 | 60 |
| Multi | 7 | 28 | 10 | 40 |
| Total | 25 | 100 | 25 | 100 |
| P | 0.5505 (Not Significant) | | | |

60-72% of the cases are primi gravida, 28-40% of the cases are multi gravida

Table 3 : Mode of Delivery

| **Mode of Delivery** | **No. of cases in** | | | |
|---|---|---|---|---|
| | **Group A** | | **Group B** | |
| | **No** | **%** | **No** | **%** |
| LSCS | 5 | 20 | 2 | 8 |
| Vaginal | 20 | 80 | 23 | 92 |
| Total | 25 | 100 | 25 | 100 |
| P | 0.2087 (Not Significant) | | | |

Mode of delivery in the two groups does not differ significantly.

In Group A, LSCS rate was 20% and group B, LSCS rate was 8%.

**Comparison of outcome parameters in the two groups**

**Table 4 : Mean Arterial Pressure**

| MAP at | Group A | | Group B | | 'p' |
|---|---|---|---|---|---|
| | **Mean** | **S.D** | **Mean** | **S.D** | |
| Admission | 118.3 | 9.6 | 123.7 | 11.0 | 0.0843 (Not Significant) |
| 12 hours | 103.6 | 7.2 | 108.9 | 5.3 | **0.005 (Significant)** |
| 24 hours | 98.6 | 6.9 | 108.9 | 5.8 | **0.0001 (Significant)** |

MAP of curettage group significantly reduced compared with controls at 12 hrs and 24 hrs after delivery

Table 5 : Urine Output

| **Urine output at** | **Group A** | | **Group B** | | **'p'** |
|---|---|---|---|---|---|
| | **Mean** | **S.D** | **Mean** | **S.D** | |
| Admission | 73.1 | 17.5 | 65.8 | 15.6 | 0.1817 (Not Significant) |
| 12 hours | 90.9 | 16.6 | 72.0 | 12.3 | **0.0001 (Significant)** |
| 24 hours | 95.2 | 7.7 | 72.7 | 14.4 | **0.0001 (Significant)** |

Rate of urine output for the curettage group was significantly more than for the non curettage group at 4 hr interval post partum. The smallest difference between both groups was observed at 12 hrs and largest at 24 hrs post partum.

**Table 6 : Platelet Count**

| Platelet count at | Group A | | Group B | | 'p' |
|---|---|---|---|---|---|
| | Mean | S.D | Mean | S.D | |
| Admission | 1.93 | 0.42 | 1.87 | 0.17 | 0.4654 (Not Significant) |
| 24 hours | 2.03 | 0.42 | 1.86 | 0.17 | 0.1441 (Not Significant) |

The platelet count of the 2 groups does not show significant difference after delivery.

**Table 7 : Urea**

| Urea at | Group A | | Group B | | 'p' |
|---|---|---|---|---|---|
| | Mean | S.D | Mean | S.D | |
| Admission | 26.8 | 9.4 | 25.9 | 6.8 | 0.9612 (Not Significant) |
| 24 hours | 24.7 | 6.1 | 25.2 | 6.0 | 0.7225 (Not Significant) |

**Table 8 : Creatinine**

| Creatinine | Group A | | Group B | | 'p' |
|---|---|---|---|---|---|
| | Mean | S.D | Mean | S.D | |
| Admission | 0.94 | 0.21 | 1.0 | 0.16 | 0.1368 (Not Significant) |
| 24 hours | 0.87 | 0.12 | 0.91 | 0.12 | 0.1427 (Not Significant) |

**Table 9 : HB %**

| HB % at | Group A | | Group B | | 'p' |
|---|---|---|---|---|---|
| | Mean | S.D | Mean | S.D | |
| Admission | 8.84 | 0.4 | 8.6 | 0.7 | 0.1392 (Not Significant) |
| 24 hours | 8.25 | 0.36 | 8.13 | 0.3 | 0.2176 (Not Significant) |

**Table 10 : Uric Acid**

| Uric acid at | Group A | | Group B | | 'p' |
|---|---|---|---|---|---|
| | **Mean** | **S.D** | **Mean** | **S.D** | |
| Admission | 6.56 | 1.82 | 5.98 | 1.35 | 0.2201 (Not Significant) |
| 24 hours | 5.69 | 1.19 | 5.4 | 1.15 | 0.1799 (Not Significant) |

Mean serum level of urea, uric acid, creatinine, hemoglobin were not significantly different between both groups at 24 hrs.

**Table 11 : Duration of Stay in MICU**

| Group | Duration of stay in MICU ( in hours) | |
|---|---|---|
| | **Mean** | **SD** |
| Group A | 55.72 | 9.57 |
| Group B | 69.37 | 12.6 |
| **'p'** | **0.0002 (Significant)** | |

The mean duration of stay in MICU was significantly shortened in curettage group compare to non curettage group.

## DISCUSSION

Resolution of pre eclampsia occurs only with delivery and subsequent removal of functioning trophoblastic tissue. As postulated by Rodgers et al and Musci et al, these trophoblastic cells produce factor that is cytotoxic to endothelial cells and in responsible for the multiplicity of clinical expression of pre eclampsia pathophysiology.

The presence of a toxin that acts as a pressor substance in the deciduas and amniotic fluid of patients with pre eclampsia has been suggested since the work of Hunter and Howard in 1960. The high decidual concentration of this substance, which they called 'hystrotonin' led these investigators to perform postpartum curettage in 70 women with preeclampsia. After curettage they observed more rapid resolution of the elevated blood pressure that accompanied pre eclampsia.

Our study, compared 2 groups of patients with eclampsia.One group underwent postpartum curettage and the other had no curettage.

1) **Maternal age:** In our study, the mean maternal age was 22.64 years in the curettage group and 22.94 years in the non curettage group. In the

study conducted by Samir Fouad Abdel Aziz, the mean age was 24.9years and 25.8 years in the curettage and non curettage groups respectively.

2) **Unbooked cases:** 92% were unbooked cases in our study. In the study by Bhargava Adarsh et al, 85.7% of the cases were unbooked. Similar findings have been reported by Chandra & Bhardwaj. Antenatal care plays a significant role in early detection and management of preeclampsia and eclampsia.

3) **Parity:** 60-72% of the cases were primigravidae and 28-40% were multigravidae, in our study. In the study by Samir Fouad Abdel Aziz, 79.2% of the parturient women were primi and 75.9% were multi.

4) **Gestational age:** The mean gestational age in our study was 31.84 weeks in the curettage group and 34.68 weeks in the non curettage group. In Bhargava Adarsh study it was 32.3 weeks and 33.5 weeks in the study and control group respectively, similar to that reported by Magann et al. In the study by Samir Fouad Abdel Aziz, it was 38.2 weeks in curettage group compared to 37.9 weeks in the non curettage group.

5) **Mode of delivery:** The LSCS rate was 20% in the curettage group compared to 8% in the control group. This is in gross variance with the Bhargava Adarsh et al study which reported 58% LSCS rate in the subjects and 68% LSCS rate in the controls.

6) **MAP:** On admission, the MAP was 124.4 mm of Hg in the subjects and 121 mm of Hg in controls in Bhargava et al, where-as it was 129.5 mm of Hg and 129.9 mm of Hg in the study by Samir Fouad Aziz. In our study the MAP in curettage and non curettage groups were 118.32 mm Hg and 123.68 mm Hg respectively.

   The MAP of the curettage group was significantly reduced compared with the controls at each 12 hours in all the above studies with the largest difference at 14 hours ($p<0.0002$) in Samir Fouad Aziz study; at 16 hours ($p<0.002$) in Bhargava Adarsh et al and 24 hours ($p<0.0001$) in our study.

7) **Urine output:** Oliguria is due to reduced renal perfusion and glomerular filtration probably resulting from reduced plasma volume. Re-establishment of an adequate urinary output is an important priority

as severe and persistent oliguria may progress to anuria, acute tubular necrosis and bilateral cortical necrosis and maternal death. An earlier and higher urine output in post partum period leads to rapid disappearance of excessive extra vascular extra cellular fluid and edema and thus to accelerated recovery of the disease process.

Urine output increased following curettage at each of the four intervals compared to that observed in the non curettage group. Mean urine output was 90.9 ml in the curettage group compared to 72.0 ml in the non curettage group. The smallest difference between both groups was observed at 12 hours and the largest difference at 24 hours postpartum ($p<0.0001$), in our study. But the smallest and the largest difference between both groups was observed in Samir Fouad Aziz study at 4 hours and 20 hours respectively ($p<0.0002$).

Both these indices, MAP and urine output reflect a more rapid resolution of preeclampsia and eclampsia and recovery from the disease process presumable via more complete removal of residual trophoblastic tissues.

8) **Platelets:** Circulating platelets were affected by uterine curettage, but

not significantly. The curettage group demonstrated an overall mean increase in platelet count from 1.93 lakhs/ml at admission to 2.03 lakhs/ml at 24 hrs post delivery. The non curettage group had a mean drop in platelet count from 1.87 lakhs/ml at admission to 1.86 lakhs/ml at 24 hrs post partum in our study. But the study by Samir Fouad Aziz reported a significant change in the platelet count with the concentration increasing from 1.59 lakhs/ml to 1.62 lakhs/ml at 24 hours postpartum in the curettage group. On contrast, the non curettage group had a decreasing platelet count from 1.48 lakhs/ml to 1.35 lakhs/ml ($p<0.05$). Drop in circulating platelets appears to be due to increased peripheral destruction produced by residual placental tissue. More rapid and complete removal of any residual placental tissue after delivery would theoretically abort much earlier the effect of any factors produced by preeclamptic placental tissue that might directly or indirectly lead to peripheral destruction of circulating platelets.

9) **Liver function tests and renal function tests:** Magann et al found no significant difference in liver function and renal function tests at 24 hours postpartum. In Bhargava et al, values of liver function and renal

function tests in subjects recorded a more rapid reversal to normal compared to those in controls. The difference in liver and renal function tests was significant at 72 hours. Witlin et al reported uric acid levels more accurately reflect the severity as well as recovery from eclampsia. In our study liver function , renal function and Hemoglobin were not significantly different in both groups. This is in par with the study by Samir Fouad Aziz which reported that uric acid, creatinine and urea levels were not significantly different in both groups at 24 hours post delivery.

Further studies are needed with longer duration to evaluate the effect of uterine curettage on these indices.

10) **Hospital stay:** Mean duration of stay in MICU was significantly shortened (52.72 hrs) in curettage group compared to non curettage group (69.37hrs), in our study. Hunter et al found an inverse relationship between the weight of the curetted deciduas and duration of stay in obstetric ICU. Average duration of stay in ICU in the study group was 51.62 hours compared to 84.16 hours in the control group in Bhargava Adarsh et al study.

## SUMMARY


- 50 women with eclampsia were selected for study, 25 as curettage group and 25 as non curettage group.
- 70% of the cases belong to age group 20-24 years
- 60-72% of the cases were primi gravida, 28-40% of the cases were multi gravida
- In curettage group LSCS rate was 20%, In non curettage group LSCS rate was 8%
- The MAP was reduced from 118.3 at admission to 103.6 at 12 hrs and 98.6 at 24 hrs in the curettage group, while it was slightly reduced in the control group. (p value – 0.0001 significant.)
- Rate of urine output increased by 45% in the curettage group while it was increased by 20% in the non curettage group at 24 hrs. (p value 0.0001)
- The mean duration of stay in MICU was 55.72 hrs in curettage group compared to prolonged 69.37 hrs in the non curettage group. (p value 0.0002)
- Platelet count, serum uric acid, urea, creatinine, Hb% were not

significantly different between both groups at 24 hrs post partum.

- Also there was no significant difference in the frequency of medications administered to either groups.
- In curettage group, none of the patients had post partum fit after delivery. In non curettage group one patient had further fits after delivery. There were no infection and haemorrhagic complications from curettage.

# CONCLUSION

Immediate puerperal uterine curettage of the parturient with eclampsia appears to accelerate disease recovery with no adverse sequelae.

Further studies involving large number of patients or multicentric studies are needed to support the accelerated disease recovery with immediate postpartum curettage.

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# PROFORMA

1. Name :
2. Age :
3. I.P. No. :
4. SEC :
5. Registration : Booked / Unbooked
6. Obstetric table :
7. Period of pregnancy :
8. Date & Time of admission :
9. Date & Time of delivery :
10. Date of Discharge :
11. Other Medical Disorder / Associated complications :
12. At the time of admission :
    - BP :
    - Urine Output :
13. USG
14. H/o AP fits : No.of fits Duration Type Consciousness BP
15. Drugs given
    - Magnesium Sulphate
    - Antihypertensives
    - Others
16. Labour
    - Spontaneous
    - Induced PGE2 Gel Oxytocin T. Misoprostol

Augmented ARM Oxytocin Both

17. Mode of delivery Vaginal Instrumental Caesarean
18. Curettage Done / Not done
19. Investigation On Admission 24hrs after delivery
    - Hb%
    - Urine Alb
    - Blood Urea
    - Sr. Creatinine
    - Sr. Uric acid
    - Sr. Bilirubin
    - Platelet count
    - Fundus
20. BP MAP Urine output Drugs
    - After delivery
    - 4 hours
    - 8 hours
    - 12 hours
    - 16 hours
    - 20 hours
    - 24 hours
21. Post partum fits
    - PPH
    - Residual HT
    - Other complications
22. Duration of stay in MICU